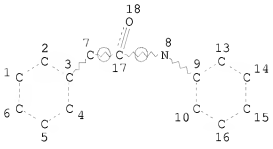
=> d l1
L1 HAS NO ANSWERS
L1 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

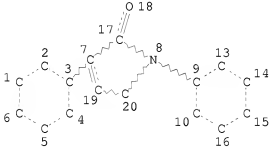
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

=> d his l3

(FILE 'REGISTRY' ENTERED AT 09:27:52 ON 26 FEB 2008)
L3 8571 S L1 FUL

=> d l16
L16 HAS NO ANSWERS
L16 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

=> d his l17

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     (FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)
L17         984 SEARCH L16 SSS  SUB=L3 FUL

=> d l18
L18 HAS NO ANSWERS
L18             STR
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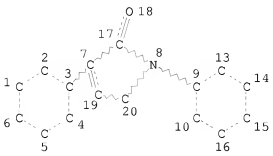


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   7
NUMBER OF NODES IS  18

STEREO ATTRIBUTES: NONE


=> d his l19

     (FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)
L19         908 SEARCH L18 SSS  SUB=L3 FUL

=> d his l20-l28

     (FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)
L20         328 S L19 AND (PYRROL?(L)DIONE)
L21         580 S L19 NOT L20
L22         125 S L21 AND (DIOXO? OR DIKETO?)
L23         455 S L21 NOT L22

     FILE 'CAPLUS' ENTERED AT 09:55:59 ON 26 FEB 2008
L24          62 S L23
L25           4 S L24 AND (DEPRES? OR ANXI? OR CNS)
L26          58 S L24 NOT L25
L27          50 S L26 AND PY<=2002
L28          21 S L27 AND P/DT

=> d bib abs l25 1-4

L25  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2006:625334  CAPLUS
DN   145:271603
TI   Diaryl substituted pyrrolidinones and pyrrolones as 5-HT2C inhibitors:
     Synthesis and biological evaluation
AU   Micheli, Fabrizio; Pasquarello, Alessandra; Tedesco, Giovanna; Hamprecht,
     Dieter; Bonanomi, Giorgio; Checchia, Anna; Jaxa-Chamiec, Albert; Damiani,
     Federica; Davalli, Silvia; Donati, Daniele; Gallotti, Chiara; Petrone,
     Marcella; Rinaldi, Marilisa; Riley, Graham; Terreni, Silvia; Wood, Martyn
```

CS GlaxoSmithKline Psychiatry Centre of Excellence for Drug Discovery, Verona, 4, 37135, Italy
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(15), 3906-3912 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
AB Within the continuous quest for the discovery of novel compds. able to treat anxiety and depression, the generation of a pharmacophore model for 5-HT2C receptor antagonists and the discovery of a new class of potent and selective 5-HT2C mols. are reported.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:1019875 CAPLUS
DN 141:406136
TI Compositions of a cyclooxygenase-2 selective inhibitor and a peroxisome proliferator activated receptor agonist for the treatment of ischemia-mediated central nervous system disorders
IN Needleman, Philip; Obukowicz, Mark G.; Arneric, Stephen P.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004100895	A2	20041125	WO 2004-US14741	20040512
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005107387	A1	20050519	US 2004-844269	20040512
PRAI	US 2003-470240P	P	20030513		

OS MARPAT 141:406136
AB The invention provides compns. and methods for the treatment of ischemia-mediated central nervous system disorders. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemia-mediated disorder comprising the administration to a subject of a peroxisome proliferator activated receptor agonist in combination with a cyclooxygenase-2 selective inhibitor.

L25 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:756686 CAPLUS
DN 141:277494
TI Preparation of diaryl substituted pyrrolidinones and pyrrolones having activity at 5-HT2c receptor
IN Damiani, Federica; Hamprecht, Dieter; Micheli, Fabrizio; Pasquarello, Alessandra; Tedesco, Giovanna
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004078718	A1	20040916	WO 2004-EP1843	20040224
	WO 2004078718	A8	20050526		
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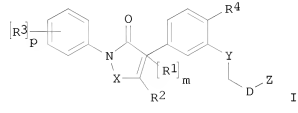
	EP 1599445	A1	20051130	EP 2004-713874	20040224
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006519241	T	20060824	JP 2006-504465	20040224
	US 2006205788	A1	20060914	US 2006-548118	20060518
PRAI	GB 2003-5024	A	20030305		
	WO 2004-EP1843	W	20040224		

OS MARPAT 141:277494
GI



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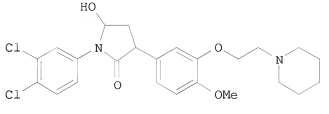

II

AB The title compds. [I; R1 = H, F, Cl, OH, alkyl, cycloalkyl, cycloalkyloxy, alkoxy or haloalkoxy; m = 0-1; R2 = H, halo, CN, NO2, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or dialkylamino or an N-linked 4-7 membered heterocyclic group; X = CH2CH2, CH:CH, (CH2)3, C(CH3)2, CH:CHCH2, CH2CH:CH or CHR5 (wherein R5 = H, halo, OH, CN, NO2, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy or alkylthio); R3 = halo, CN, alkyl, cycloalkyl, cycloalkyloxy, alkoxy, alkylthio, OH, NH2, mono- or dialkylamino, etc.; p = 0-3; R4 = H, halo, OH, CN, NO2, alkyl, alkanoyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or dialkylamino or an N-linked 4-7 membered heterocyclic group; Y = O, S, CH2 or NR10 (wherein R10 = H, alkyl); D = a single bond, CH2, (CH2)2 or CH:CH; Z = NR11R12 (where R11 and R12 = H, alkyl, (un)substituted N-linked or C-linked 4-7 membered

heterocyclic group)] and their pharmaceutically acceptable salts, useful in treating, for example, depression and anxiety, were prepared E.g., a multi-step synthesis of II, was given. All exemplified compds. I were tested for their affinity for the 5-HT2c receptor, and were found to have pKi values >5.8. The pharmaceutical composition comprising the compound I is disclosed.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:855908 CAPLUS
DN 139:350638
TI 3-Aryl-1-[4-alkoxy-3-[2-(piperidin-1-yl)ethoxy]phenyl]pyrrolidin-2-ones and analogs with affinity at 5-HT2C receptors, and use thereof in therapy, particularly as antidepressants and anxiolytics, and their preparation and pharmaceutical compositions
IN Damiani, Federica; Hamprecht, Dieter; Jaxa-Chamiec, Albert Andrzej; Micheli, Fabrizio; Pasquarello, Alessandra; Tedesco, Giovanna
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003089409	A1	20031030	WO 2003-EP4180	20030417
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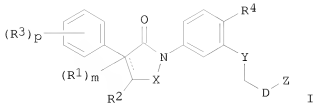
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003222832	A1	20031103	AU 2003-222832	20030417
	EP 1497265	A1	20050119	EP 2003-718783	20030417
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005529117	T	20050929	JP 2003-586130	20030417
	US 2005203079	A1	20050915	US 2005-511769	20050502
PRAI	GB 2002-9029	A	20020419		
	GB 2002-20781	A	20020906		
	WO 2003-EP4180	W	20030417		

OS MARPAT 139:350638
GI



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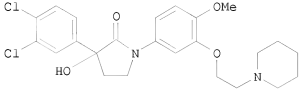

II

AB Title compds. I and their pharmaceutically acceptable salts are disclosed [wherein: R1 = H, OH, F, Cl, alkyl, cycloalkyl, cycloalkyloxy, alkoxy or haloalkoxy; m = 0 or 1; R2 = H, halo, cyano, NO2, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or di-C1-6alkylamino, or N-linked 4-7 membered heterocyclic; X = CH2CH2, CH:CH, (CH2)3, C(CH3)2, CH:CHCH2, CH2CH:CH, or CHR5; R3 = halo, cyano, alkyl, cycloalkyl, cycloalkyloxy, C1-6alkoxy, C1-6alkylthio, OH, amino, mono- or di-C1-6alkylamino, N-linked 4-7 membered heterocyclic, NO2, haloalkyl, haloalkoxy, aryl, arylalkyl, arylalkyloxy, arylalkylthio, COOR6, CONR7R8, or COR9; R4 = H, halo, OH, cyano, NO2, alkyl, alkanoyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or di-alkylamino or N-linked 4-7 membered heterocyclic; R5 = H, halo, OH, cyano, NO2, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy or alkylthio; R6, R7, R8, and R9 = H or alkyl; p = 0, 1, 2, or 3; Y = O, S, CH2, or NR10; R10 = H or alkyl; D = bond, CH2, (CH2)2, or CH:CH; Z = (un)substituted C-linked 4-7 membered heterocyclic group containing at least 1 N, (un)substituted N-linked 4-7 membered heterocyclic, or Z = NR11R12; R11 and R12 = H or alkyl]. Methods of preparation and uses of I in therapy, particularly for treating CNS disorders such as depression and anxiety, are also disclosed. The affinities of compds. I for 5-HT2C receptors were determined by assessing their ability to displace [3H]-mesulergine from rat or human 5-HT2C clones expressed in 293 cells in vitro, as described in WO 94/04533. All example compds. were so tested and had pKi values >5.8. Some compds. I show a considerably higher affinity, in the range of 7.0 to >9.0 in human cells. Approx. 45 synthetic examples and approx. 75 precursor prepns. are given. For instance, 3,4-dichlorophenylacetic acid underwent a sequence of (1) α-lithiation and allylation, (2) amidation with 2-(5-amino-2-methoxyphenoxy)ethyl acetate, (3) OsO4-catalyzed glycolation of the alkene, and periodate oxidation of the glycol with cyclic hemiaminal formation, to give a 5-hydroxy-2-pyrrolidinone derivative, (4) reduction of the latter to remove 5-hydroxy, (5) saponification of the acetate ester sidechain to an alc., (6) conversion of the alc. to a mesylate ester, and (7) aminolysis of the mesylate with piperidine in the presence of K2CO3 and NaI, followed by benzylic hydroxylation with air over 18 h, to give title compound II.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT